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Original Scientific Paper

Changes in lipid profile of patients referred to a cardiac rehabilitation program

Nizal Sarrafzadegan[a], Katayoun Rabiei[b], Ali Kabir[c], Seddighe Asgary[d], Aliakbar Tavassoli[g], Alireza Khosravi[e] and Hamid Chalian[f]

[a]Department of Medicine, WHO Collaborating Center, [b]Rehabilitation Department, [c]Practical Studies Department, Nikan Health Researchers Institute, [d]Basic Research Department, [e]Department of Cardiology, High Risk Unit, Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, [f]Nikan Health Researchers Institute and [g]Department of Cardiology, Medical University of Isfahan, Tehran, Iran

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Background **Cardiac rehabilitation program (CRP) has been demonstrated to have beneficial effects on physical and mental functioning as well as on mortality of patients with cardiovascular diseases, but its exact effect on lipid profile of these patients is still vague. In this study we aimed to evaluate the effect of comprehensive CRP on lipid profile of the Iranian population.**

Design **Self-controlled descriptive study.**

Methods **We evaluated 547 patients with documented coronary heart disease before and after a 24-session CRP between 1998 and 2003. Some of them received antilipid drugs.**

Results **Except for diastolic blood pressure, all other biophysical, biochemical [total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride (TG)], functional, and psychosocial parameters had significant response to CRP. We can attribute the normalization of lipid in these patients to CRP in combination with medications 34.9% for TC, 17.7% for LDL, and 27.2% for TG ($P<0.001$ for all). Antilipid drugs had some more effect in normalizing the TC (9.7%), LDL (1.8%), and TG (7.3%).**

Conclusion **Comprehensive CRP improves TC, TG, LDL, and HDL in Iranian patients with cardiovascular disease even without antilipid drugs, and antilipid therapy can boost this effect.** *Eur J Cardiovasc Prev Rehabil* **15:467–472 © 2008 The European Society of Cardiology**

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Introduction

Cardiovascular disease (CVD) is the leading cause of death in Iran, which accounts for 46% of overall mortality [1]. The rapid increase in coronary artery disease in Iran and many other developing countries in the world is associated with marked changes in life style regarding diet and physical activity over the past two decades [2,3]. It has been demonstrated previously that Iran has some remarkable features regarding CVD, as the Iranian population has a greater risk for CVD than most other populations, especially due to higher lipid risk factors [4].

An extensive literature on the effects of lipids on atherosclerosis progression is available [5]. The importance of cholesterol lowering has been well documented in the past both in primary and secondary prevention strategies for reducing cardiovascular risk factors in some studies [6].

Cardiac rehabilitation programs (CRPs), first developed in the 1960s [7,8], have been shown to have beneficial effects on mortality, exercise tolerance, functional capacity, lipid levels, blood pressure, symptoms of angina and

Correspondence to Ali Kabir, MD, Methodology and Statistics Consultant, Isfahan Cardiovascular Research Center; Head of Practical Studies Department of Nikan Health Researchers Institute, Unit #9, no. 1, 3rd Bahar Street, Ashrafi Esfahani Exp way, Poonak Square, Tehran, Iran
Tel: +98 21 66516995, +98 21 44468645; fax: +98 21 44476796;
e-mail: aikabir@yahoo.com

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dyspnea, weight loss, smoking behavior, stress level, and psychosocial functioning [9–12]. However, there are some controversies over the effect of CRP on different types of serum lipids [13–16], and racial differences have been mentioned in the degree of improvement of patients' lipid profile after CRP [17]. Considering the selective effect of lipid-lowering drugs on different types of serum lipids and the importance of lipid lowering in the management of patients with cardiovascular diseases, it seems vital to clarify the exact effect of CRP on different types of serum lipids for better selection of these drugs for patients completing a CRP. As up till now, no investigation has been performed to evaluate changes in lipid profile after CRP in the Iranian population, we conducted a self-controlled observational study to evaluate the changes in lipid profile of the Iranian patients completing a comprehensive CRP, whether receiving antilipid medications or not.

Patients and methods

Study population and assessments

In a backward self-controlled observational study between 1998 and 2003, we evaluated 1220 patients with coronary heart disease (CHD); they were referred to cardiac rehabilitation (CR) department of the Isfahan Cardiovascular Research Center by cardiology, interventional and cardiac surgery departments. No selection criteria existed, except for CR contraindication such as unstable angina, acute phase of myocardial infarction (MI), and unstable arrhythmia. Inclusion criteria consisted completeness of 24 sessions of CRP irrespective of antilipid medications use.

Patients had a history of MI, coronary artery bypass graft, percutaneous coronary intervention, percutaneous transluminal coronary angioplasty (PTCA) or CHD evidenced by angiography. All of the patients with MI started outpatient CR after 4 weeks of acute MI. In coronary artery bypass graft patients, the duration between surgery and the start of CR is 6–8 weeks, depending on the surgeon's opinion. In the percutaneous coronary intervention patients CR should be started as soon as possible.

A checklist was completed for the patients at the time of admission according to medical history and physical examination by trained general practitioners, physiotherapists and nurses. It addressed demographic variables, reason for referral to CR, the date of enrollment, CHD risk factors, height, weight, waist and hip circumference, systolic and diastolic blood pressures (SBP and DBP), heart rate (HR), and drugs. Waist-to-hip ratio was calculated according to National Heart, Lung, and Blood Institute (NHLBI) recommendations [18].

To determine functional capacity, patients did a Naughton exercise test under the supervision of a cardiologist, without withholding the patients' medications [19]. In addition, to determine left ventricular ejection fraction (LVEF), a transthorasic echocardiography was done by the cardiologists.

A blood sample was taken after 12–14 h of fasting to measure fasting blood sugar, serum lipids including triglyceride (TG), and total cholesterol (TC) using enzymatic colorimetric methods. High-density lipoprotein (HDL) was determined after dextran sulphate-magnesium chloride precipitation of non-HDL cholesterol; then, low-density lipoprotein (LDL) was calculated according to Friedewald formula [20]. All tests were measured at the beginning of the study.

Risk stratification of the patients (low, intermediate, and high) was done by the cardiologists on the basis of exercise test and LVEF [21].

In our study, medications which were prescribed to patients were categorized to (i) directly affecting lipid level [clofibrate, gemfibrazil, lovastatine, fluvastatine, simvastatin, atrovastatin, nicotinic acid (niacin), cholesteramin], (ii) indirectly affecting lipid levels (glucocorticoids, thiazide, β-blocker, valproate and related drugs, garlic, estrogen and progesterone) [22,23], and (iii) having no effect on lipids. Normal range of lipids is considered as TG < 150, LDL < 100, and TC < 200 for both men and women.

Rehabilitation program and follow-up

The rehabilitation program comprised 24 exercise sessions, scheduled over 8 weeks. Each session took 60–90 min, beginning with a 10–20 min warm-up followed by 20–40 min aerobic exercise, and was terminated with a 10 min cool-down. In addition, there was a 20 min relaxation at the end of each session.

The intensity of the exercise was calculated according to the determined risk, between 60 and 85% of the maximum HR achieved on the exercise test [21]. The exercise was done under electrocardiographic monitoring if the patient was at high risk.

All patients received the psychological, nutritional, and smoking cessation consultations. In addition, there were weekly educational sessions during the 8 weeks of CRP, both for patients and their families. It consisted of explanations on cardiovascular diseases, introducing risk factors, diagnoses and treatment approaches, medications and their complications, stress reduction methods, and advices on the healthy life style including smoking cessation, nutrition, and physical activity.

For all patients who completed the whole CRP, the tests were reconducted at the end of the study.

Data processing, analysis and ethical consideration

Mean ± SE, paired *t*-test, one-way analysis of variance, Pearson and McNemar χ^2 were used in analysis. General linear model was used for counterbalance the confounder effect of quantitative dependent variables. Logistic regression was utilized to adjust for the confounding effects of qualitative variables. Stepwise multivariate linear regression model was used with Pearson correlation coefficient (r) to detect independent variables that can predict changes in important dependent variables. Differences and correlations with $P < 0.05$ were considered statistically significant. SPSS 13 software (SPSS Inc., Chicago, Illinois, USA) was used in analysis.

The study protocol was reviewed and approved by Isfahan Cardiovascular Research Center Ethical Committee, which is a member of the Office for Human Research Protections, US, Department of Health and Human Services, with the assurance number: FWA00008578.

Results

A total of 547 patients [400 (males (73.1%)] entered the study. The remaining 653 patients (44.8%) dropped out from CR. Table 1 shows their baseline characteristics.

Table 1 Basic characteristics of men and women patients referred to CRP

Variables	Description
Demographics	
Age (year, mean ± SE)	55.8 ± 0.39
Job [no. (%)]	
Self-employed	154 (28.2%)
Employed	127 (23.2%)
Retired	115 (21%)
Homemaker	124 (22.7%)
Worker	12 (2.2%)
Jobless	15 (2.7%)
Married [no. (%)]	533 (97.4%)
Educational level [no. (%)]	
Illiterate	170 (31.4%)
Primary school	151 (27.9%)
Secondary school	137 (25.3%)
Master's degree and higher	84 (15.4%)
Income (Toomans/month, mean ± SE)	130 533 ± 5663
Reason for refer [no. (%)]	
CABG	312 (57%)
MI	120 (22%)
PCI	52 (9.5%)
Abnormal angiography	11 (2%)
Others	52 (9.5%)
Risk factors [no. (%)]	
Hypertension[a]	175 (32.1%)
Dyslipidemia[a]	286 (52.4%)
Family history	269 (49.2%)
Smoking	45 (8.2%)
Diabetes[a]	132 (24.1%)
History of obesity	218 (39.9%)
Present BMI (mean ± SE)	27.2 ± 0.16
Sedentary life style	196 (44.6%)
Risk stratification [no. (%)]	
Low risk	350 (64%)
Intermediate	97 (17.7%)
High risk	100 (18.3%)

BMI, body mass index; CABG, coronary artery bypass graft; CRP, cardiac rehabilitation program; MI, myocardial infarction; PCI, percutaneous coronary interventions. [a]History of, or being on treatment for risk factor.

Table 2 Response to cardiac rehabilitation program

Variables	Before CRP (mean ± SE), *N*	After CRP (mean ± SE), *N*	Significant value
Weight (kg)	73.1 ± 0.47, 547	71.5 ± 0.46, 542	<0.001
BMI (kg/m^2)	27.2 ± 0.16, 547	26.6 ± 0.16, 542	<0.001
Waist circumference (cm)	99.3 ± 0.44, 546	96.3 ± 0.44, 536	<0.001
Hip circumference (cm)	104.2 ± 0.32, 546	101.4 ± 0.31, 536	<0.001
Waist-to-hip ratio	0.95 ± 0.003, 546	0.95 ± 0.003, 536	0.006
Serum lipoprotein levels (mg/dl)			
TC	225.2 ± 2.1, 544	206.7 ± 1.9, 547	<0.001
LDL	144.2 ± 1.8, 504	127.5 ± 1.6, 523	<0.001
HDL	39.8 ± 0.38, 536	40.8 ± 0.37, 543	0.014
TG	218 ± 5.4, 545	192.5 ± 3.98, 547	<0.001
FBS (mg/dl)	107.7 ± 1.68, 545	104.2 ± 1.29, 542	0.005
Functional capacity (Mets)	9 ± 0.12, 543	11.2 ± 0.13, 546	<0.001
LVEF (%)	50.3 ± 0.51, 518	54.1 ± 0.46, 447	<0.001
SBP (mmHg)	124.8 ± 0.96, 547	121.9 ± 0.83, 546	0.003
DBP (mmHg)	75.9 ± 0.53, 547	75 ± 0.48, 546	0.1
HR (per min)	83 ± 0.78, 531	79.9 ± 0.74, 526	<0.001
Depression score	4.3 ± 0.19, 534	2.87 ± 0.12, 534	<0.001
Anxiety score	17.1 ± 0.59, 526	15.5 ± 0.53, 526	<0.001

BMI, body mass index; CRP, cardiac rehabilitation program; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; HR, heart rate; LDL, low-density lipoprotein; LVEF, left ventricle ejection fraction; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

Response to CRP according to physical, biochemical, functional, and psychosocial parameters are mentioned in Table 2. It showed that except for DBP, all other parameters had significant improvement.

Level of TG was normalized (difference between patients with abnormal levels at the beginning and end of the study) in 44 patients (8.1%), LDL in 40 patients (8.2%), and TC in 77 patients (14.1%). Percents of patients with abnormal TG, LDL, and TC that have a normal value at the end of follow-up were 50.2, 67.3 and 49.4%, respectively. However, there were some patients with normal level of lipid profile initially who had an abnormal value at the end of the study. This was 17.8, 9, and 17.4% for TG, LDL, and TC, respectively. All of these changes were significant ($P < 0.001$).

Statins were mostly used in comparison with the other lipid-lowering medications. [245 (44.8%) vs. 37 (6.8%) patients] By adjusting for the effect of lipid-lowering medications, CRP decreased the value of lipids significantly for TC, LDL, and TG and increased the amount of HDL in patients who had not used antilipid medications too (Table 3).

No significant difference between final value of lipids of patients with and without using antilipid medications was observed. Patients without antilipid drugs, however, had lower HDL ($P < 0.001$) and higher TC ($P = 0.01$) before CRP (Table 3).

We can attribute the normalization of lipid in these patients to CRP in combination with medications 34.9% for TC, 17.7% for LDL, and 27.2% for TG ($P < 0.001$ for all). Antilipid drugs had some more effects in normalizing the TC (9.7%), LDL (1.8%), and TG (7.3%). Stepwise linear regression showed significant models for predicting

Table 3 Comparison of response to cardiac rehabilitation program in patients with and without (CRP only) antilipid drugs

Variables	Before CRP (mean ± SE), *N*	After CRP (mean ± SE), *N*	Significant value
Serum lipoprotein levels in patients with antilipid drugs (mg/dl)			
TC	230.9 ± 3.2, 257	205.5 ± 2.8, 257	<0.001
LDL	147.8 ± 2.7, 231	125.9 ± 2.4, 231	<0.001
HDL	41.2 ± .5, 256	41.4 ± 0.5, 256	NS
TG	222.5 ± 8.4, 258	187.7 ± 5.9, 258	<0.001
Serum lipoprotein levels in patients without antilipid drugs (mg/dl)			
TC	220.2 ± 2.7, 288	207.9 ± 2.4, 288	<0.001
LDL	141.4 ± 2.4, 258	129.3 ± 2.2, 258	<0.001
HDL	38.5 ± 0.5, 277	40.2 ± 0.5, 277	0.001
TG	213.9 ± 7, 288	196.9 ± 5.4, 288	0.002

CRP, cardiac rehabilitation program; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

Table 4 Multivariate stepwise linear regression analysis for predicting final values of lipids

Dependent variables	Independent variables	*B*	Significant value
LDL	TC before CRP	0.346	<0.001
	Income	−0.152	0.001
	Age	0.096	0.028
HDL	HDL before CRP	0.426	<0.001
	Functional capacity before CRP	−0.137	<0.001
	Smoking[a]	−0.102	0.009
TG	TG before CRP	0.584	<0.001
	Smoking[a]	0.160	<0.001
	BMI before CRP	0.099	0.005
Cholesterol	TC before CRP	0.788	<0.001
	Functional capacity before CRP	−0.149	<0.001
	LDL before CRP	−0.331	<0.001
	Hip circumference before CRP	0.134	0.001

[a]Nonsmoker multiplied by 1 and smoker by 2. *B*, slope of linear regression; BMI, body mass index; CRP, cardiac rehabilitation program; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

changes in LDL ($P < 0.001$, $R^2 = 0.183$), HDL ($P < 0.001$, $R^2 = 0.224$), TG ($P < 0.001$, $R^2 = 0.401$), and TC ($P < 0.001$, $R^2 = 0.343$) (Table 4).

It showed that lower LDL, higher income, and lower age would independently lead to lower final LDL after CRP. Higher HDL, lower functional capacity, and not being a smoker before CRP would lead to higher final HDL. Patients with lower TG, lower body mass index (BMI), and not being a smoker before CRP would have lower final TG. Finally, if a person had lower TC and hip circumference and higher functional capacity and LDL before CRP, he/she would have lower TC after CRP (Table 4).

Discussion

In this study, we found that comprehensive CRP (including physical activity, psychological, nutritional, and smoking cessation consultations) and drug therapy improved all assessed biophysical, biochemical, functional, and psychosocial parameters including weight, BMI, waist circumference, hip circumference, waist-to-hip ratio, fasting blood glucose, functional capacity, LVEF, SBP, HR, depression, and anxiety scores except DBP. In this investigation, CRP and antilipid therapy showed to improve TC, LDL, HDL, and TG. We also found that improvement of HDL can be attributed to CRP alone (without antilipid therapy).

Inability of CRP in improving DBP while reducing SBP in a significant manner has been demonstrated in previous trials [13]. Positive effect of CRP on body weights and sizes has also been demonstrated by many authors previously [17,24,25].

Exact effect of CRP on lipid profile of patients with cardiovascular diseases is still a matter of debate. This evaluation seems much more crucial in Iran. As it has been reported that the Iranian population have much higher CVD risk factors such as LDL, TC, and physical inactivity in comparison with the US and Europe [26]. It has also been reported that, based on the Rose Q and/or ECG, the prevalence of CVD was significantly higher among Iranian women than Iranian men [27]. In a prospective study in which patients who received lipid-lowering drugs were excluded, The HDL and LDL fractions did not change significantly after completion of a CRP including a combination of general dietary advice and moderate physical exercise training [16], whereas others have reported that CRP can improve LDL, HDL, and TG in patients with CVD [15]. In other investigations, the increases in HDL after completion of CRP have been demonstrated to be similar to those associated with drug therapy [28]. In a systematic review and meta-analysis of randomized controlled trials evaluating the outcomes of exercise-based CRP, it has been illuminated that CRP was associated with a significant reduction in TC and TG levels whereas there seemed not to be a significant difference in LDL and HDL cholesterol levels after completion of CRP [13].

Within our literature review, there is a paucity of assessments that have evaluated the simultaneous effect of CRP and antilipid medications on patients' lipid levels, and instead have weighted their results according to the effect of CRP and drugs separately. In an assessment, measurement of lipid levels at enrollment in a CRP and subsequently at regular intervals, with aggressive lipid-lowering therapy, in consultation with the primary care physician, has demonstrated to triple the use of drug therapy and significantly reduced LDL levels [29]. In our investigation, TC, TG, HDL, and LDL levels improved significantly after comprehensive CRP and antilipid therapy. Analysis of our data demonstrated that CRP could reduce the levels of TC, TG, HDL, and LDL significantly, even without using antilipid medication. This was in line with an investigation showed that home-based cardiac exercise program reduced TC, TG, HDL, and LDL compared with the control group [30].

Comparison of the results of two groups (with and without pharmacological therapy), showed that signifi-

cant increase of HDL is due to CRP alone and decrease of TC, LDL, and TG was because of CRP with or without antilipid drugs. The finding that antilipid therapy could not improve HDL level, in this study, may be due to the fact that in our study population, patients who received antilipid therapy had higher basal levels of HDL. The reason for the finding that antilipid therapy was not effective enough to improve serum lipids (especially LDL and TC) to the normal range may be low compliance of our physicians and patients with antilipid drugs [31]. It has been demonstrated in many investigations that acceptance of pharmacological treatment for elevated lipids has been low. In the EuroAspire study, less than 50% of patients received appropriate lipid-lowering therapy after a cardiac event [32]. Under nonstudy conditions, this percentage is probably even lower as in the primary care settings [33], cardiology practices [34], and academic centers [35] many patients with established coronary artery disease are not treated with statins or other lipid-lowering agents. Numerous attempts have been made to improve compliance with the National Cholesterol Education Program treatment guidelines [36]. We suggest that a CRP should be considered as an appropriate opportunity for improving patients' compliance with antilipid therapy. As education of the patients is a main component of a comprehensive CRP, CRPs should emphasize the need to adhere to the appropriate medical regimen, in addition to the nonpharmacological treatment modalities of CR, to achieve better risk-reducing result.

In this investigation, regression models showed independent factors for predicting the post-CRP values of lipid profile. It showed that baseline level of lipids, income, age, functional capacity, not being a smoker, BMI, and hip circumference were the most important predictors. Future studies may be able to show which of these independent factors can constantly be entered in regression models. These models can be used as practical guidelines for the most useful interventions.

In our study, only 45% of patients who had entered the CRP completed the course. For the remaining 55% of patients, we could not check lipid profiles at the end of the CRP duration which made us unable to evaluate the isolated effect of antilipid drugs in our population. In this investigation, we did not assess our patients' compliance with the medications that they were using during CRP including antilipid drugs. We suggest that this is assessed in future studies for evaluating the effect of CRP on patients' compliance with drugs and better clarification of CRP outcomes. High rate of drop out of patients can be a potential source of selection bias in our study.

Conclusion

This study showed the favorable effect of CRP on lipid profile (including TC, TG, HDL, and LDL) of patients with CVD. We also demonstrated that this effect happened even without the use of lipid-lowering drugs. Although, we suggest that for achieving the most favorable impact on lipid levels in patients with CVD, a multifactorial CRP that include exercise training, dietary education, and psychological support and counseling should also include educational sessions on the importance of pharmacological as well as nonpharmacological treatments of serum lipids.

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References

1 Iranian Ministry of Health and Medical Education: a national survey on health and diseases in Iran. Report; 2000.
2 World Health Organization. Technical report series 894. Obesity, preventing and managing the global epidemic. Report of a WHO consultation. Geneva' World Health Organization; 2000.
3 Ghassemi H, Harrison G, Mohammad K. An accelerated nutrition transition in Iran. *Public Health Nutr* 2002; **5**:149–155.
4 Jalali BA, Rafie M, Mozaffari H. Lipoprotein (A) as a strong risk factor for coronary artery disease in Iranian population. *Med J Islamic Acad Sci* 2000; **13**:5–9.
5 Wierzbicki AS. Lipid-altering therapies and the progression of atherosclerotic disease. *Cardiovasc Intervent Radiol* 2007; **30**:155–160.
6 Nadar S, Lim HS, Beevers DG, Lip GY. Lipid lowering in hypertension and heart protection: observations from the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) and the Heart Protection Study. *J Hum Hypertens* 2002; **16**:815–817.
7 Wenger N, Hellerstein HK, Blackburn H, Castranova SJ. Uncomplicated myocardial infarction: current physician practice in patient management. *JAMA* 1973; **224**:511–514.
8 Hellerstein HK. Exercise therapy in coronary disease. *Bull N Y Acad Med* 1968; **44**:1028–1047.
9 Mosca L, Manson JE, Sutherland SE, Langer R, Manolio T, Barrett-Connor E. Cardiovascular disease in women: a statement for healthcare professionals from the American Heart Association. *Circulation* 1997; **96**:2468–2482.
10 Wenger N, Froelicher E, Smith L. Cardiac rehabilitation as secondary prevention. Clinical practice guideline 96–0673 1995; Rockville: US, Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, and National Heart, Lung, and Blood Institute.
11 Carhart R, Ades P. Gender differences in cardiac rehabilitation. *Cardiol Clin* 1998; **16**:37–43.
12 Taylor RS, Unal B, Critchley JA, Capewell S. Mortality reductions in patients receiving exercise-based cardiac rehabilitation: how much can be attributed to cardiovascular risk factor improvements? *Eur J Cardiovasc Prev Rehabil* 2006; **13**:369–374.
13 Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, *et al*. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004; **116**:682–692.
14 Ades PA. Cardiac rehabilitation and secondary prevention of coronary heart disease. *N Engl J Med* 2001; **345**:892–902.
15 Lavie CJ, Milani RV. Factors predicting improvements in lipid values following cardiac rehabilitation and exercise training. *Arch Intern Med* 1993; **153**:982–988.
16 Baardman T, Fioretti P, van Tol A, Erdman RA, van Meurs-van Woezik H, Kazemier M. Changes in plasma lipoproteins after cardiac rehabilitation in patients not on lipid-lowering drugs. *Eur Heart J* 1990; **11**:722–729.
17 Sanderson BK, Mirza S, Fry R, Allison JJ, Bittner V. Secondary prevention outcomes among black and white cardiac rehabilitation patients. *Am Heart J* 2007; **153**:980–986.
18 Harris T, Cook EF, Garrison R, Higgins M, Kannel W, Goldman L. Body mass index and mortality among nonsmoking older persons. *JAMA* 1988; **259**:1520–1524.

19 Jennings S, Carey D. Capacity and equity in cardiac rehabilitation in the eastern region: good and bad news. *Ir J Med Sci* 2004; **173**:151–154.

20 Friedewald WT, Levy RI, Fridrikson DS. Estimation of concentrations of low-density lipoprotein cholesterol in plasma without use of preparative ultracentrifuge. *Clin Chem* 1972; **18**:499–502.

21 Pashkow FJ, Dafoe WA. *Clinical cardiac rehabilitation 2nd education*. Baltimore: Williams and Wilkins; 1999. pp. 137–147, 458-466.

22 Brunzell JD. Hypertriglyceridemia. *NEJM* 2007; **357**:1009–1017.

23 Kojuri J, Vosoughi AR, Akrami M. Effects of anethum graveolens and garlic on lipid profile in hyperlipidemic patients. *Lipids Health Dis* 2007; **6**:5.

24 Yates BC, Heeren BM, Keller SM, Agrawal S, Stoner JA, Ott C. Comparing two methods of rehabilitation for risk factor modification after a cardiac event. *Rehabil Nurs* 2007; **32**:15–22.

25 Höfer S, Kullich W, Graninger U, Brandt D, Gassner A, Klicpera M, *et al*. Cardiac rehabilitation in Austria: short term quality of life improvements in patients with heart disease. *Wien Klin Wochenschr* 2006; **118**:744–753.

26 Hatmi ZN, Tahvildari S, Ghafarzadeh Motlag A, Sabouri Kasnani A. Prevalence of coronary artery disease risk factors in Iran: a population based survey. *BMC Cardiovasc Disord* 2007; **7**:32.

27 Sarraf-Zadegan N, Sayed-Tabatabaei FA, Bashardoost N, Maleki A, Totonchi M, Habibi HR, *et al*. The prevalence of coronary artery disease in an urban population in Isfahan, Iran. *Acta Cardiol* 1999; **54**:257–263.

28 Rubins HB, Robins SJ, Collins D, Fye CL, Anderson JW, Elam MB, *et al*. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. *N Engl J Med* 1999; **341**:410–418.

29 Ades PA, Savage PD, Poehlman ET, Brochu M, Fragnoli-Munn K, Carhart RL Jr. Lipid lowering in the cardiac rehabilitation setting. *J Cardiopulm Rehabil* 1999; **19**:255–260.

30 Senuzun F, Fadiloglu C, Burke LE, Payzin S. Effects of home-based cardiac exercise program on the exercise tolerance, serum lipid values and self-efficacy of coronary patients. *Eur J Cardiovasc Prev Rehabil* 2006; **13**:640–645.

31 Mendis S, Abegunde D, Yusuf S, Ebrahim S, Shaper G, Ghannem H, Shengelia B. WHO study on Prevention of REcurrences of Myocardial Infarction and StrokE (WHO-PREMISE). *Bull World Health Organ* 2005; **83**:820–829.

32 EUROASPIRE Study Group (Wood DA for the). EUROASPIRE–A European Society of Cardiology survey of secondary prevention of coronary heart disease: principal results. *Eur Heart J* 1997; **18**:1569–1582.

33 McBride P, Schrott HG, Plane MB, Underbakke G, Brown RL. Primary care practice adherence to National Cholesterol Education Program guidelines for patients with coronary heart disease. *Arch Intern Med* 1998; **158**:1238–1244.

34 Sueta CA, Chowdhury M, Boccuzzi SJ, Smith SC Jr, Alexander CM, Londhe A, *et al*. Analysis of the degree of undertreatment of hyperlipidemia and congestive heart failure secondary to coronary artery disease. *Am J Cardiol* 1999; **83**:1303–1307.

35 European Action on Secondary Prevention by Intervention to Reduce Events. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. EUROASPIRE I and II group. *Lancet* 2001; **357**:995–1001.

36 LaBresh KA, Ellrodt AG, Gliklich R, Liljestrand J, Peto R. Get with the guidelines for cardiovascular secondary prevention: pilot results. *Arch Intern Med* 2004; **164**:203–209.